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MAMSSGGSGGGVPEQEDSVLFRRGTGQSDDSDIWDDTALIKAYDKAVAS
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PATIASIDFKRETCVVVYTGYGNREEQNLSDLLSPICEVANNIEQNAQENENESQVSTDE
SENSRSPGNKSDNIKPKSAPWNSFLPPPPPMPGPRLGPGKPGLKFNGPPPPPPPPPPHLL
SCWLPPFPSGPPIIPPPPPICPDSLDDADALGSMLISWYMSGYHTGYYMGFRQNQKEGRC
SHSLN

FIGURE 1

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CGGGGCCCCACGCTGCGCACCCGCGGGTTTGCTATGGCGATGAGCAGCGGCGGCAGTGGT
GGCGGCGTCCCGGAGCAGGAGGATTCCGTGCTGTTCCGGCGCGGCACAGGCCAGAGCGAT
GATTCTGACATTTGGGATGATACAGCACTGATAAAAGCATATGATAAAGCTGTGGCTTCA
TTTAAGCATGCTCTAAAGAATGGTGACATTTGTGAAACTTCGGGTAAACCAAAAACCACA
CCTAAAAGAAAACCTGCTAAGAAGAATAAAAGCCAAAAGAAGAATACTGCAGCTTCCTTA
CAACAGTGGAAAGTTGGGGACAAATGTTCTGCCATTTGGTCAGAAGACGGTTGCATTTAC
CCAGCTACCATTGCTTCAATTGATTTTAAGAGAGAAACCTGTGTTGTGGTTTACACTGGA
TATGGAAATAGAGAGGAGCAAAATCTGTCCGATCTACTTTCCCCAATCTGTGAAGTAGCT
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TGGAACCCCTTTCTCCCTCCACCACCCCCCATGCCAGGGCCAAGACTGGGACCAGCAAAG
CCAGGTCTAAAATTCAATGGCCCACCACCGCCACCGCCACCACCACCACCCCACTTACTA
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TGTCCAGATTCTCTTGATGATGCTGATGCTTTGGGAAGTATGTTAATTTCATGGTACATG
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TCACATTCCTTAAATTAAGGAGAAATGCTGGCATAGAGCAGCACTAAATGACACCACTAA
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TCTGTAAAAGACTGAGGTGGGGGTGGGAGGCCAGCACGGTGGTGAGGCAGTTGAGAAAAT
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GTGGCAAAATGTTACAGAATCTAACTGGTGGACATGGCTGTTCATTGTACTGTTTTTTTC
TATCTTCTATATGTTTAAAAGTATATAATAAAAATATTTAATTTTTTTTTTAAAAAAAAAA
AAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAA
AAAAAAAAAAAAAAAAAAAAAA

FIGURE 2A

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AATTTTTAAATTTTTTGTAGAGACAGGGTCTCATTATGTTGCCCAGGGTGGTGTCAAGCTCCA
GGTCTCAAGTGATCCCCCTACCTCCGCCTCCCAAAGTTGTGGGATTGTAGGCATGAGCCACTG
CAAGAAAACCTTAACTGCAGCCTAATAATTGTTTTCTTTGGGATAACTTTTAAAGTACATTAA
AAGACTATCAACTTAATTTCTGATCATATTTTGTTGAATAAAATAAGTAAAATGTCTTGTGAA
CAAAATGCTTTTTTAACATCCATATAAAGCTATCTATATATAGCTATCTATATCTATATAGCTA
TTTTTTTTTAACTTCCTTTTATTTTCCTTACAG*GGTTTCAGACAAAATCAAAAAGAAGGAAGG
TGCTCACATTCCTTAAATTAAGGA*GTAAGTCTGCCAGCATTATGAAAGTGAATCTTACTTTT
GTAAAACTTTATGGTTTGTGGAAAACAAATGTTTTTGAACAGTTAAAAAGTTCAGATGTTAGA
AAGTTGAAAGCTTAATGTAAAACAATCAATATTAAAGAATTTTGATGCCAAAACTATTAGATA
AAAGGTTAATCTACATCCCTACTAGAATTCTCATACTTAACTGGTTGGTTGTGTGGAAGAAAC
ATACTTTCACAATAAAGAGCTTTAGGATATGATGCCATTTTATATCACTAGTAGGCAGACCAG
CAGACTTTTTTTTTATTGTGATATGGGATAACCTAGGCATACTGCACTGTACACTCTGACATAT
GAAGTGCTCTAGTCAAGTTTAACTGGTGTCCACAGAGGACATGGTTTAACTGGAATTCGTCAA
GCCTCTGGTTCTAATTTCTCATTTGCAG*GAAATGCTGGCATAGAGCAGCACTAAATGACACC
ACTAAAGAAACGATCAGACAGATCTGGAATGTGAAGCGTTATAGAAGATAACTGGCCTCATTT
CTTCAAAATATCAAGTGTTGGGAAAGAAAAAAGGAAGTGGAATGGGTAACTCTTCTTGATTA
AAAGTTATGTAATAACCAAATGCAATGTGAAATATTTTACTGGACTCTTTTGAAAAAC
CATCTGTAAAAGACTGGGGTGGGGGTGGGAGGCCAGCACGGTGGTGAGGCAGTTGAGAAAA
TTTGAATGTGGATTAGATTTTGAATGATATTGGATAATTATTGGTAATTTTATGGCCTGT
GAGAACGGTGTTGTAGTTTATAAAACACTGTCTTAATTTGCATACTTAAGCATTTAGG
AATGAAGTGTTAGAGTGTCTTAAAATGTTTCAAATGGTTTAACAAAATGTATGTGAGGCGT
ATGTGGCAAAATGTTACAGAATCTAACTGGTGGACATGGCTGTTCATTGTACTGTTTTTT
TCTATCTTCTATATGTTTAAAAGTATATAATAAAAATATTTAATTT

FIGURE 2B

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1

CGGGGCCCCACGCTGCGCATCCGCGGGTTTGCTATGGCGATGAGCAGCGGCGGCAGTGGT

2

GGCGGCGTCCCGGAGCAGGAGGATTCCGTGCTGTTCCGGCGCGGCACAGGCCAG*ACCGAT

GATTCTGACATTTGGGATGATACAGCACTGATAAAAGCATATGATAAAGCTGTGGCTTCA

TTTAAGCATGCTCTAAAGAATGGTGACATTTGTGAAACTTCGGGTAAACCAAAAACCACA

CCTAAAAGAAAACCTGCTAAGAAGAATAAAAGCCAAAAGAAGAATACTGCAGCTTCCTTA

3

CAACAG*TGGAAAGTTGGGGACAAATGTTCTGCCATTTGGTCAGAAGACGGTTGCATTTAC

CCAGCTACCATTGCTTCAATTGATTTTAAGAGAGAAACCTGTGTTGTGGTTTACACTGGA

TATGGAAATAGAGAGGAGCAAAATCTGTCCGATCTACTTTCCCCAATCTGTGAAGTAGCT

4

AATAATATAGAACAGAATGCTCAAGAG*AATGAAAATGAAAGCCAAGTTTCAACAGATGAA

AGTGAGAACTCCAGGTCTCCTGGAAATAAATCAGATAACATCAAGCCCAAATCTGCTCCA

TGCAACTCTTTTCTCCCTCCACCACCCCCCATGCCAGGGCCAAGACTGGGACCAGGAAAG

5

*CCAGGTCTAAAATTCAATGGCCCACCACCGCCACCGCCACCACCACCACCCCACTTACTA

6

TCATGCTGGCTGCCTCCATTTCCTTCTGGACCACCA*ATAATTCCCCCACCACCTCCCATA

TGTCCAGATTCTCTTGATGATGCTGATGCTTTGGGAAGTATGTTAATTTCATGGTACATG

7

AGTGGCTATCATACTGGCTATTATATG*GGTTTCAGACAAAATCAAAAAGAAGGAAGGTGC

8

TCACATTCCTTAAATTAAGGA*GAAATGCTGGCATAGAGCAGCACTAAATGACACCACTAA
AGAAACGATCAGACAGATCTGGAATGTGAAGCGTTATAGAAGATAACTGGCCTCATTTCT
TCAAAATATCAAGTGTTGGGAAAGAAAAAAGGAAGTGGAATGGGTAACTCTTCTTGATTA
AAAGTTATGTAATAACCAAATGCAATGTGAAATATTTTACTGGACTCTTTTGAAAAAC
CATCTGTAAAAGACTGGGGTGGGGGTGGGAGGCCAGCACGGTGGTGAGGCAGTTGAGAAAA
TTTGAATGTGGATTAGATTTTGAATGATATTGGATAATTATTGGTAATTTTATGGCCTGT
GAGAAGGGTGTTGTAGTTTATAAAAGACTGTCTTAATTTGCATACTTAAGCATTTAGG
AATGAAGTGTTAGAGTGTCTTAAAATGTTTCAAATGGTTTAACAAAATGTATGTGAGGCGT
ATGTGGCAAAATGTTACAGAATCTAACTGGTGGACATGGCTGTTCATTGTACTGTTTTTT
TCTATCTTCTATATGTTTAAAAGTATATAATAAAAATATTTAATTTTTTTTTAAAAAAAA
AAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAA

FIGURE 3A

AATTTTTAAATTTTTTGTAGAGACAGGGTCTCATTATGTTGCCCAGGGTGGTGTCAAGCTCCA
GGTCTCAAGTGATCCCCCTACCTCCGCCTCCCAAAGTTGTGGGATTGTAGGCATGAGCCACTG
CAAGAAAACCTTAACTGCAGCCTAATAATTGTTTTCTTTGGGATAACTTTTAAAGTACATTAA
AAGACTATCAACTTAATTTCTGATCATATTTTGTTGAATAAAATAAGTAAAATGTCTTGTGAA
CAAAATGCTTTTTTAACATCCATATAAAGCTATCTATATATAGCTATCTATGTCTATATAGCTA
TTTTTTTTAACTTCCTTTTATTTTCCTTACAG*GGTTTCAGACAAAATCAAAAAGAAGGAAGG
TGCTCACATTCCTTAAATTAAGGA*GTAAGTCTGCCAGCATTATGAAAGTGAATCTTACTTTT
GTAAAACTTTATGGTTTGTGGAAAACAAATGTTTTTGAACAGTTAAAAAAGTTCAGATGTTAAA
AAGTTGAAAGGTTAATGTAAAACAATCAATATTAAAGAATTTTGATGCCAAAACTATTAGATA
AAAGGTTAATCTACATCCCTACTAGAATTCTCATACTTAACTGGTTGGTTATGTGGAAGAAAC
ATACTTTCACAATAAAGAGCTTTAGGATATGATGCCATTTTATATCACTAGTAGGCAGACCAG
CAGACTTTTTTTTTATTGTGATATGGGATAACCTAGGCATACTGCACTGTACACTCTGACATAT
GAAGTGCTCTAGTCAAGTTTAACTGGTGTCCACAGAGGACATGGTTTAACTGGAATTCGTCAA
GCCTCTGGTTCTAATTTCTCATTTGCAG*GAAATGCTGGCATAGAGCAGCACTAAATGACACC
ACTAAAGAAACGATCAGACAGATCTGGAATGTGAAGCGTTATAGAAGATAACTGGCCTCATTT
CTTCAAAATATCAAGTGTTGGGAAAGAAAAAAGGAAGTGGAATGGGTAACTCTTCTTGATTA
AAAGTTATGTAATAACCAAATGCAATGTGAAATATTTTACTGGACTCTTTTGAAAAAC
CATCTGTAAAAGACTGGGGTGGGGGTGGGAGGCCAGCACGGTGGTGAGGCAGTTGAGAAAA
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ATGTGGCAAAATGTTACAGAATCTAACTGGTGGACATGGCTGTTCATTGTACTGTTTTTT
TCTATCTTCTATATGTTTAAAAGTATATAATAAAAATATTTAATTT

FIGURE 3B

C212

ACCTGANCCCAGANGGTCAAGGCTGCAGTGAGACGAGATTGCNCCACTGCCCTCC
ACCCTGGGTCATAAGAGTGGGACCCTGTNTCAAAACATACACACACACACACACA
CACACACACACACACACACACACACTCTCTCTCTCTCTCTCTCTCTCTCTCTCTC
TCTCTCTCTCTCTCAAAAACACTTGGTCTGTTATTTTTNCGAAATTGTCAGTCAT
AGTTATCTGTTAGACCAAAGCTGNGTAAGNACATTTATTACATTGCCTCCTACAA
CTTCATCAGCTAATGTATTTGCTATATAGCAATTACATATNGGNATATATTATCT
TNAGGGGATGGCCANGTNATAAAACTGTCACTGAGGAAAGGA

C272

CCTCCCACCTNAGCCTCCCCAGTAGCTAGGACTATAGGCGTGCNCCACCAAGCTC
AGCTATTTTTNNTATTTAGTAGAGACGGGGTTTCGGCANGCTTAGGCCTCGTNTC
GAACTCCAGTGTGTGTGTGTGTGTGTGTGTGTGTGTGTGTGTGTGTGTGTGTG
TGTGTAGATATTTATTCCCCCTCCCCCTTGGAAAAGTAAGTAAGCTCCTACTAGG
AATTTAAAACCTGCTTGATCTATATAAAGACAAACAAGGAAAGACAAACATGGGG
GCAGGAAGGAAGGCAGATC

AFM157xd10

TCGAGGTAGATTTGTATTATATCCCATGTACACACACACACACACACACACAC
ACACACACACACAGACTTAATCTGTTTACAGAAATAAAAGGAATAAAATACCGTT
TCTACTATACACCAAAACTAGCCATCTTGAC

C161

CCCTGAGAAGGCTTCCTCCTGAGTATGCATAAACATTCACAGCTTGCATGCGTGT
GTGTGTGTGTGTGTGTGTGTATGTTTGCTTGCACTGTAAAAACAATTGCAACATC
AACAGAAATAAAAATTAAAGGAATAATTCTCCTCCGACTCTGCCGTTCCATCCAG
TGAAACTCTTCATTCTGGGGTAAAGTTCCTTCAGTTCTTTCATAGATAGGTATAT
ACTTCATAAGTCAAACAATCAGGCTGGGTGCAGTAGCTCATGCCTGTAATCCCAG
CCCTTTGGGAGGCCGAGCTGGGCAGATCGA

C171

TCCACCCGCCTTGGCCTCCCAAAGCNCTGGGATTACAGGCGTCACTGCCGCACCC
AGCTGTAAACTGGNTTNNTAATGGTAGATTTTNAGGTATTAACAATAGATAAAAA
GATACTTTTNGGCATACTGTGTATTGGGATGGGGTTAGAACAGGTGTNCTACCCA
AGACATTTACTTAAAATCGCCCTCGAAATGCTATGTGAGCTGTGTGTGTGTGTGT
GTGTGTGTGTGTATTAAGGAAAAGCATGAAAGTATTTATGCTTGATTTTTTTTTT
TNACTCATACCTTCATAGTGGANCAGATACATAGTCTAAATCAAAATGTTTAAAC
TTTTTATGTCACTTGCTGTC

FIGURE 4

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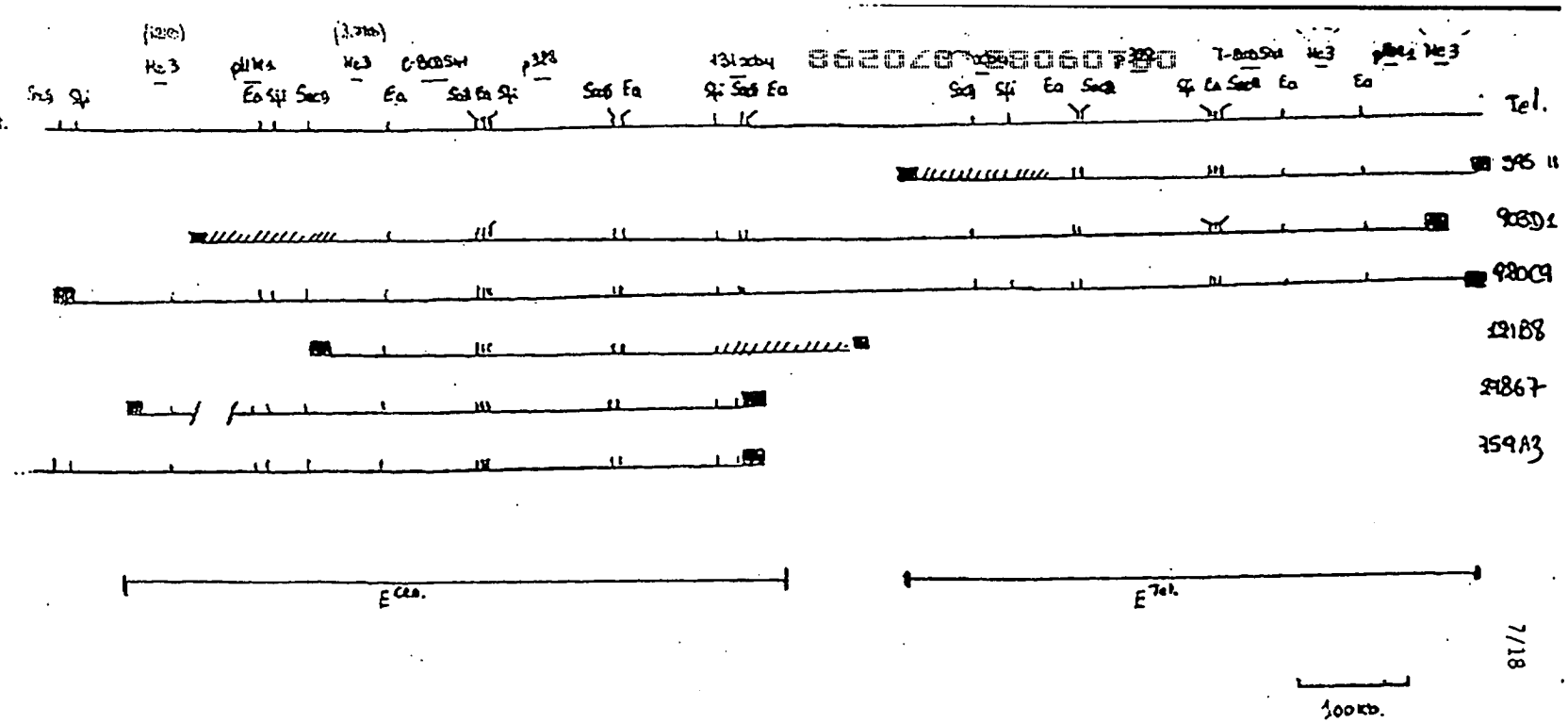
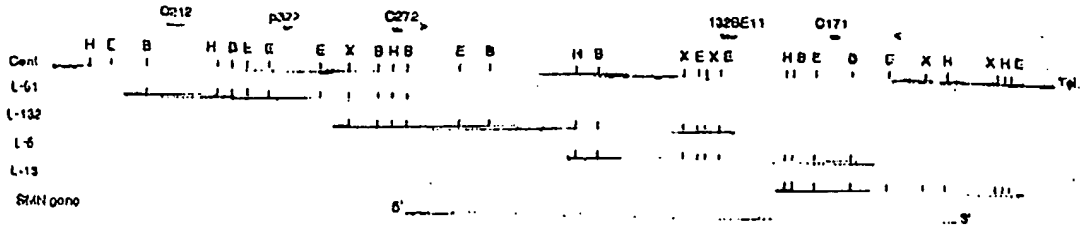


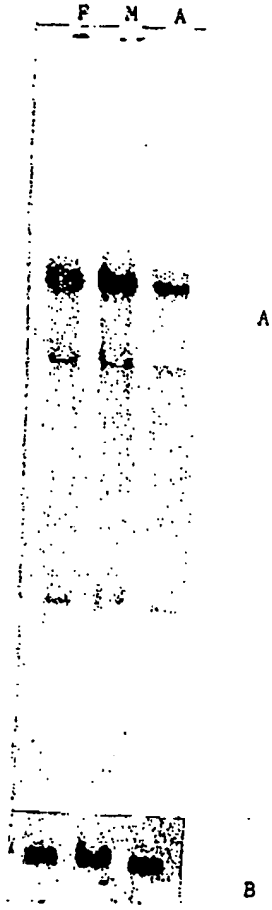
FIGURE 5

Restriction map of the 5q13 region. for Eag I (Ea), Sac II (Sac II), Sfi I (Sfi). Numbers under parentheses indicate the restriction fragment detected by He3; Telomeric element (E^{Tel}), centromeric element ($E^{Cen.}$) Centromere (Cent.), Telomere (Tel.). Probes are indicated above the restriction map. YACs are below the restriction map.



Telomeric element (E^{Tel}) containing the survival motor-neuron gene (SMN gene). Genetic map shows polymorphic markers C212, C272 and C171. Physical map shows location and direction of transcription of SMN gene; phage clones used for assembling physical map. Restriction map for EcoRI(E), XbaI(X), HindIII(H), BglII(B), SacII(S) are shown. Cent. and Tel. indicate centromere and telomere respectively. The position of genomic rearrangements found in SMA patients are also indicated.

FIGURE 6



Gene dosage analysis of the 5q13 region with the 132SE11 plasmid cone in SMA type I patient. Total human DNA from SMA family was digested with HindIII for Southern blotting. Filter was consecutively hybridized with 132SE11 (A) and JK53 probes (B). A significant decrease in 132SE11 band intensity, which indicated the deletion, compared with their parents. F/Father, M/Mother, A/affected

FIGURE 7

MAMSSGGSGGGVPEQEDSVLFRRGTGQSDDSDIWDDTALIKAYDKAVASFKHA
LKNGDICETSGKPKTTPKRKPAKKNKSQKKNTAASLQQWKVGDKCSAIWSEDG
CIYPATIASIDFKRETCVVVYTGYGNREEQNLSDLISPICEVANNIEQNAQEN
ENESQVSTDESENSRSPGNKSDNIKPKSAPWNSFLPPPPPPMPGPRLGPGKPGL
KFNGPPPPPPPPPPPHLISCWLPPFPSGPPIIPPPPPICPDSLDDADALGSMLI
SWYMSGYHTGYYM

FIGURE 8

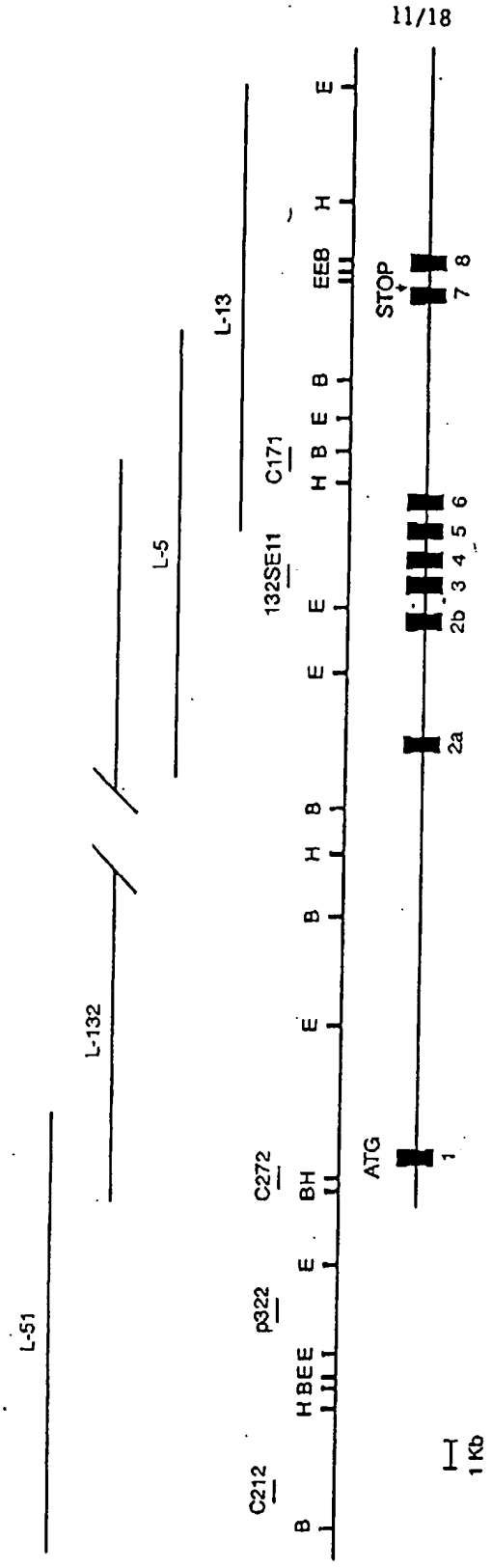

L-51
L-132
L-5
L-13
C212
B
H B E E
p322
E
C272
B H
E
B
H
B
E
E
132SE11
C171
H B E B
EEB
H
E
ATG
1
2a
2b 3 4 5 6
STOP
7 8
1 Kb

Figure 9

WO 95/30745

```
1
cctcccgggcaccgtactgttccgctcccagaagccccgggcgccggaaglcgtcactcttaagaagggacg
gggccccacgctgcgcacccgcgggtttgct ATG GCG ATG AGC AGC GGC GGC AGT GGT GGC
                                 M  A  M  S  S  G  G  S  G  G
GGC GTC CCG GAG CAG GAG GAT TCC GTG CTG TTC CGG CGC GGC ACA GGC CAG gtg
 G   V   P   E   Q   E   D   S   V   L   F   R   R   G   T   G   Q
aggtcgcagccagtgcagtctccctattagcgctctcagcaccctttcttccggcccaactctccttccgca
2a
gtgtaattttgttatgtgtggattaagatgactcttggtactaacatacattttctgattaaacctatctgn
acatgagttgttttattttcttacccttttccag AGC GAT GAT TCT GAC ATT TGG GAT GAT
                                  S   D   D   S   D   I   W   D   D
ACA GCA CTG ATA AAA GCA TAT GAT AAA GCT GTG GCT TCA TTT AAG gtatgaaatgc
 T   A   L   I   K   A   Y   D   K   A   V   A   S   F   K
ttgnttagtcgttttcttatttttctcgttattcatttggaaaggaattgataacatacgataaagtgttaa
2b
aggtgctttctgagglgacggagccttgagactagcttatagtagtaactgggttatgtcgtgacttttatt
ctgtgcaccaccctgtaacatgtacatttttattcctatttttcgtag CAT GCT CTA AAG AAT GGT
                                                 H   A   L   K   N   G
GAC ATT TGT GAA ACT TCG GGT AAA CCA AAA ACC ACA CCT AAA AGA AAA CCT GCT
 D   I   C   E   T   S   G   K   P   K   T   T   P   K   R   K   P   A
AAG AAG AAT AAA AGC CAA AAG AAG AAT ACT GCA GCT TCC TTA CAA CAG gttattt
 K   K   N   K   S   Q   K   K   N   T   A   A   S   L   Q   Q
taaaatgttgaggatttaacttcaaaggatgtctcattagtccttatttaatagtgtaaaatgtctttaact
3
gcctgcaggtcgatcaaaacgagatgatagtttgccctcttcaaaagaaatgtgtgcatgtatatatctttg
atttcttttgtag TGG AAA GTT GGG GAC AAA TGT TCT GCC ATT TGG TCA GAA GAC
              W   K   V   G   D   K   C   S   A   I   W   S   E   D
GGT TGC ATT TAC CCA GCT ACC ATT GCT TCA ATT GAT TTT AAG AGA GAA ACC TGT
 G   C   I   Y   P   A   T   I   A   S   I   D   F   K   R   E   T   C
GTT GTG GTT TAC ACT GGA TAT GGA AAT AGA GAG GAG CAA AAT CTG TCC GAT CTA
 V   V   V   Y   T   G   Y   G   N   R   E   E   Q   N   L   S   D   L
CTT TCC CCA ATC TGT GAA GTA GCT AAT AAT ATA GAA CAG AAT GCT CAA GAG gta
 L   S   P   I   C   E   V   A   N   N   I   E   Q   N   A   Q   E
aggatacaaaaaaaaaaaaattcaatttctggaagcagagactagatgagaaactgttaaacagtatacaca
4
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AAT GAA AAT GAA AGC CAA GTT TCA ACA GAT GAA AGT GAG AAC TCC AGG TCT CCT
 N   E   N   E   S   Q   V   S   T   D   E   S   E   N   S   R   S   P
GGA AAT AAA TCA GAT AAC ATC AAG CCC AAA TCT GCT CCA TGG AAC TCT TTT CTC
 G   N   K   S   D   N   I   K   P   K   S   A   P   W   N   S   F   L
CCT CCA CCA CCC CCC ATG CCA GGG CCA AGA CTG GGA CCA GGA AAG gtaaaccttct
 P   P   P   P   P   M   P   G   P   R   L   G   P   G   K
atgaaagttttccagaaaatagttaatgtcgggacatttaacctctctgttaactaatttgtagctctccca
5
caaatattctgggtaattatttttatcctttggttttgagtcctttttattcctatcatattgaaattggt
aagttaatttttcctttgaaatattccttatag CCA GGT CTA AAA TTC AAT GGC CCA CCA CCG
                                 P   G   L   K   F   N   G   P   P   P
CCA CCG CCA CCA CCA CCA CCC CAC TTA CTA TCA TGC TGG CTG CCT CCA TTT CCT
 P   P   P   P   P   P   P   H   L   L   S   C   W   L   P   P   F   P
TCT GGA CCA CCA  gtaagtaaaaaagagtataggttagattttgctttcacatacaatttgataatta
 S   G   P   P
6
ccagacttactttttgtttactggatataaacaatatcttttctgtctccag ATA ATT CCC CCA
                                                      I   I   P   P
CCA CCT CCC ATA TGT CCA GAT TCT CTT GAT GAT GCT GAT GCT TTG GGA AGT ATG
 P   P   P   I   C   P   D   S   L   D   D   A   D   A   L   G   S   M
TTA ATT TCA TGG TAC ATG AGT GGC TAT CAT ACT GGC TAT TAT ATG gtaagtaatca
 L   I   S   W   Y   M   S   G   Y   H   T   G   Y   Y   M
ctcagcatcttttcctgacaatttttttglagttatgtgactttgtttggtaaatttataaaatactacttg
```

Figure 10

7
aactgcagcctaataattgttttctttgggataacttttaaagtacattaaaagactatcaacttaatttct
gatcatattttgttgaataaaataagtaaaatgtcttgtgaaacaaaatgcttttaacatccatataaagc
→ a
tatctatatatagctatctatgtctatatagctatttttttaactttttttcattttccttacag GGT
→ T G
TTC AGA CAA AAT CAA AAA GAA GGA AGG TGC TCA CAT TCC TTA AAT taaggagtaag
F R Q N Q K E G R C S H S L N *
tctgccagcattatgaaagtgaatcttactttgtaaactttatggtttgtggaaaacaaatgtttttgaa
→ g
cagttaaaaagttcagatgttaaaaagttgaaaggttaatgtaaaacaatcaatattaaagaattttgatgc
→ g
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→ a
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tgaatgtggattagattttgaatgatattggataattattggtaattttatggcctgtgagaagggtgttgt
agtttataaaagactgtcttaatttgcatacttaagcatttaggaatgaagtgttagagtgtcttaaaatgt
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Figure 10 (Continued)

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                                H4TF-1      GH
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                                DTF-1
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                                               Sp1
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                  β-IFN                                         HiNF-A
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cctcccgggcaccgtactgttccgctcccagaagccccgggcgccggaagtcgtcagtcttaagaagggacg  576
                                   AP-2          E4F1
gggccccacgctgcgcacccgcgggtttgct ATG GCG ATG AGC AGC GGC GGC AGT GGT GGC  637
                                 M   A   M   S   S   G   G   S   G   G
```

Figure 11

cggcgtggtegcaggcc ATG GCG ATG GGC AGT GGC GGA GCG GGC TCC GAG CAG GAA 58
Met Ala Met Gly Ser Gly Gly Ala Gly Ser Glu Gln Glu

GAT ACG GTG CTG TTC CGG CGT GGC ACC GGC CAG AGT GAT GAT TCT GAC ATT TGG 112
Asp Thr Val Leu Phe Arg Arg Gly Thr Gly Gln Ser Asp Asp Ser Asp Ile Trp

GAT GAT ACA GCA TTG ATA AAA GCT TAT GAT AAA GCT GTG GCT TCC TTT AAG CAT 166
Asp Asp Thr Ala Leu Ile Lys Ala Tyr Asn Lys Ala Val Ala Ser Phe Lys His

GCT CTA AAG AAC GGT GAC ATT TGT GAA ACT CCA GAT AAG CCA AAA GGC ACA GCC 220
Ala Leu Lys Asn Gly Asp Ile Cys Glu Thr Pro Asp Lys Pro Lys Gly Thr Ala

AGA AGA AAA CCT GCC AAG AAG AAT AAA AGC CAA AAG AAG AAT GCC ACA ACT CCC 274
Arg Arg Lys Pro Ala Lys Lys Asn Lys Ser Gln Lys Lys Asn Ala Thr Thr Pro

TTG AAA CAG TGG AAA GTT GGT GAC AAG TGT TCT GCT GTT TGG TCA GAA GAC GGC 328
Leu Lys Gln Trp Lys Val Gly Asp Lys Cys Ser Ala Val Trp Ser Glu Asp Gly

TGC ATT TAC CCA GCT ACT ATT ACG TCC ATT GAC TTT AAG AGA GAA ACC TGT GTC 382
Cys Ile Tyr Pro Ala Thr Ile Thr Ser Ile Asp Phe Lys Arg Glu Thr Cys Val

GTG GTT TAT ACT GGA TAT GGA AAC AGA GAG GAG CAA AAC TTA TCT GAC CTA CTT 436
Val Val Tyr Thr Gly Tyr Gly Asn Arg Glu Glu Gln Asn Leu Ser Asp Leu Leu

TCC CCG ACC TGT GAA GTA GCT AAT AGT ACA GAA CAG AAC ACT CAG GAG AAT GAA 490
Ser Pro Thr Cys Glu Val Ala Asn Ser Thr Glu Gln Asn Thr Gln Glu Asn Glu

AGT CAA GTT TCC ACA GAC GAC AGT GAA CAC TCC TCC AGA TCG CTC AGA AGT AAA 544
Ser Gln Val Ser Thr Asp Asp Ser Glu His Ser Ser Arg Ser Leu Arg Ser Lys

GCA CAC AGC AAG TCC AAA GCT GCT CCG TGG ACC TCA TTT CTT CCT CCA CCA CCC 598
Ala His Ser Lys Ser Lys Ala Ala Pro Trp Thr Ser Phe Leu Pro Pro Pro Pro

CCA ATG CCA GGT [illegible] GGA TTA GGA CCA GGA AAG CCA GGT CTA AAA TTC AAC GGC 652
Pro Met Pro Gly Asn Gly Leu Gly Pro Gly Lys Pro Gly Leu Lys Phe Asn Gly

CCG CCG CCG [illegible] CCT CCA CTA [illegible] CCT CCC [illegible] TTC CTG [illegible] TG[illegible] TGG ATG CCC 706
Pro Pro Pro Pro Pro Pro Leu Pro Pro Pro Pro Phe Leu Pro Cys Trp Met Pro

CCG TTC CCT TCA GGT CCA CCA ATA ATC CCG CCA CCC CCT CCC ATC TCT CCC GAC 760
Pro Phe Pro Ser Gly Pro Pro Ile Ile Pro Pro Pro Pro Pro Ile Ser Pro Asp

TGT CTG GAT [illegible] ACT GAT [illegible] CT[illegible] GGC AGT ATG CTA ATC TCT TGG TAC ATG AGT 814
Cys Leu Asp Asp Thr Asp Ala Leu Gly Ser Met Leu Ile Ser Trp Tyr Met Ser

GGC TAC CAC [illegible] [illegible] TAC TAT ATG GGT TTC AGA CAA AAT AAA AAA GAA GGA AAG 868
Gly Tyr His Thr Gly Tyr Tyr Met Gly Phe Arg Gln Asn Lys Lys Glu Gly Lys

TGC TCA CAT ACA AAT TGA
Cys Ser His Thr Asn * 887

Figure 12

```
 20          30          40          50          60          70          80
GSGGGVPEQEDSVLFRRGTGQSDDSDIWDDTALIKAYDKAVASFKHALKNGDICETSGKPKTTPKRKPAK
GSGGAGSEQEDTVLFRRGTGQSDDSDIWDDTALIKAYDKAVASFKHALKNGDICETPDKPKGTARRKPAK
          20          30          40          50          60          70

 90         100         110         120         130         140         150
KNKSQKKNTAASLQQWKVGDKCSAIWSEDGCIYPATIASIDFKRETCVVVYTGYGNREEQNLSDLLSPIC
KNKSQKKNATTPLKQWKVGDKCSAVWSEDGCIYPATITSIDFKRETCVVVYTGYGNREEQNLSDLLSPTC
          90         100         110         120         130         140

160         170         180         190         200         210         220
EVANNIEQNAQENFNESQVSTDESENSRSPGNKSDNIKPKSAPWNSFLPPPPPMPGPRLGPGKPGLKFNG
EVANSTEQNTQENE--SQVSTDDSEHSSRSLRSKAHSKSKAAPWTSFLPPPPPMPGSGLGPGKPGLKFNG
          160         170         180         190         200         210

230         240         250         260         270         280         290
PPPPPPPPPPHLLSCWLPPFPSGPPIIPPPPPICPDSLDDADALGSMLISWYMSGYHTGYYMGFRQNQKE
PPPPPPLPPPPFLPCWMPPFPSGPPIIPPPPPISPDCLDDTDALGSMLISWYMSGYHTGYYMGFRQNKKE
220         230         240         250         260         270         280

300
GRCSHSL
GKCSHTN
290
```

Figure 13

09160582.072998

0520720 2606760

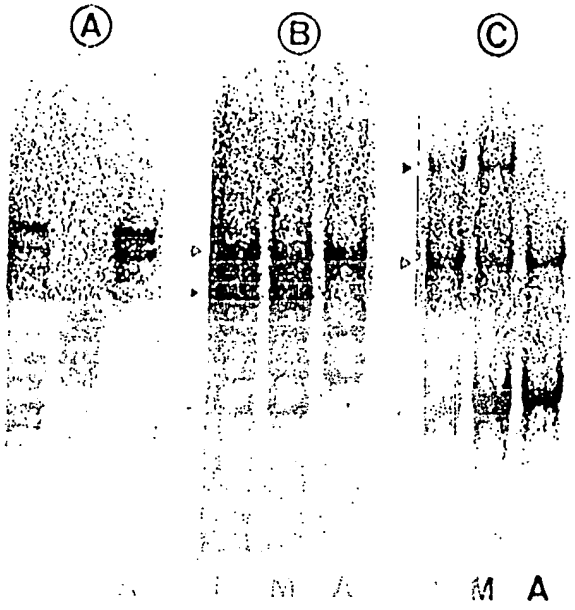
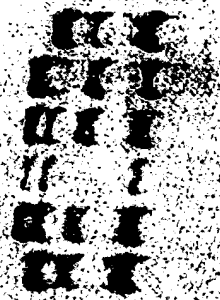


Figure 14

SSCP Analysis

▼ SMN

▽ C-BCD541



421B8 YAC

595C11 YAC

HUMAN 1 CONTROL

HUMAN 2 CONTROL

HUMAN 3 CONTROL

HUMAN 4 SMA

Figure 15